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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/737,542	12/14/2000	Robin R. Miles	IL-10406	9714

7590 06/28/2004

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EXAMINER	
PADMANABHAN, KARTIC	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 06/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/737,542	MILES ET AL.	
	Examiner	Art Unit	
	Kartic Padmanabhan	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/14/04 has been entered.

Terminal Disclaimer

2. The terminal disclaimer filed on 6/14/04 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on US Application No. 09/993,870 has been reviewed and is accepted. The terminal disclaimer has been recorded.

3. The terminal disclaimer filed on 6/14/04 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on US Application No. 09/738,927 has been reviewed and is accepted. The terminal disclaimer has been recorded.

4. The terminal disclaimer filed on 6/14/04 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent No. 6,437,551 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 10, 12-18, and 21-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Gerwen et al. (WO 97/21094) in view of Nelson et al. (US Pat. 6,074,827).

Van Gerwen et al. teach an impedimetric detection system comprising an insulating layer with a plurality of interspersed channels therein. A metal coating is applied to one of the two opposite side walls of each channel and on top of the dielectric layer in between said channels, thereby forming an impedimetric device. Probes are applied to either the insulating part of the channels or to the surface of the electrodes or both (abstract). The device also comprises means

for applying a voltage on the metal coatings and measuring the impedance between the electrodes. The sensor of the reference also has an interdigitated electrode structure (page 10, lines 10-16 and page 15, line 28). The probes of the device include antibodies (page 5 and figures 1-7). When an electric signal is applied (voltage or current), an electric field arises. If the analyte is present in the solution tested, it will be bound to the probe on the electrode surface, resulting in a change in impedance, which is then quantified (page 15). It is inherent that the means for producing the electric field is an AC or DC power supply. However, the reference does not teach pairs of electrodes located on the same surface and/or same side of the microchannel or on a bottom surface of the channel, nor does it teach antibody-coated beads.

Nelson et al. teach microfluidic purification and separation methods, wherein beads coated with antibodies specific for the analyte of interest are used to bind the target analyte and separate it from the rest of the sample (Col. 6, lines 30-45).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to place the electrode pair on the same side of the microchannel, since it has been held that rearranging parts of an invention involves only routine skill in the art. *In re Japikse*, 86 USPQ 70. In addition, the placement of the electrodes on a bottom surface of the microchannel would have been obvious because it simply represents an optimization of the device or a rearrangement of the parts of the device, which one would have had a reasonable expectation of success in using. In addition, it would have been obvious to use the antibody-coated beads of Nelson et al. with the device of Van Gerwen et al. because Nelson teaches the use of these coated beads in fluidic systems having channels, and the use of these beads to bind the pathogens of

Van Gerwen would allow for an even more noticeable difference in the impedance measurements between when pathogen is present and when it is not.

9. Claims 10, 12-13, 16, and 20-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark et al. (US Pat. 5,194,133) in view of Kipling et al. (US Pat. 5,374,521) and Nelson et al. (US Pat. 6,074,827).

Clark et al. teach sensor devices comprising pairs of sensing electrodes that are spaced apart along the walls of a channel that has been micromachined in a surface of a substrate (abstract). The channel walls may be coated with a biological substance, such as an enzyme (col. 1). The electrodes may be amperometric enzyme electrodes (Col. 3, lines 48-50). The sensors of the reference may be used to measure impedance between electrodes (col. 5, lines 50-55). A DC pulse may be used generate the electric field (col. 5, lines 60-65). The reference also teaches a plurality of signal generators and a plurality of amplifier/mixer assemblies (Figure 6). The reference does not teach antibodies located on the electrodes.

Kipling et al. teach a sensor comprising a pair of spaced electrodes that may both have a coating attached thereto (col. 1). A receptor will be attached to the coating on the electrodes, and the receptor may any biomolecule, including antibodies (col. 5). A voltage is applied between the electrodes, which makes it inherent that there is a means for applying this voltage to create an electric field (col. 3). The impedance between the electrodes is one of the parameters that can be determined with the sensor of the reference (col. 5). It is further inherent that the electric field is produced by an AC or DC power supply because these power supplies are generally used to apply voltages at various frequencies. However, the reference does not teach antibody-coated beads.

Nelson et al. teach microfluidic purification and separation methods, wherein beads coated with antibodies specific for the analyte of interest are used to bind the target analyte and separate it from the rest of the sample (Col. 6, lines 30-45).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the antibodies on the surfaces of the electrode as taught by Kipling et al. with the device of Clark et al. because Kipling teaches that any number of biomolecules can be used on the electrode surface. Therefore, depending on the analyte one wishes to detect, one would have known that a number of receptors could have been placed on the electrodes of Clark et al. with a reasonable expectation of success. In addition, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to place the electrode pair on the same side of the microchannel, since it has been held that rearranging parts of an invention involves only routine skill in the art. *In re Japikse*, 86 USPQ 70. Also, the placement of the electrodes on a bottom surface of the microchannel would have been obvious because it simply represents an optimization of the device or a rearrangement of the parts of the device, which one would have had a reasonable expectation of success in using. It would have further been obvious to use the antibody-coated beads of Nelson et al. with the modified device of Clark et al. and Kipling et al. because Nelson teaches the use of these coated beads in fluidic systems having channels, and the use of these beads to bind the pathogens of interest would allow for an even more noticeable difference in the impedance measurements between when pathogen is present and when it is not.

10. Claims 11, 14, 17-19, and 27-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark et al. (US Pat. 5,194,133) in view of Kipling et al. (US Pat. 5,374,521)

and Nelson et al. (US Pat. 6,074,827) as applied to claims 10, 12-13, 16, and 20-21 above, and further in view of Taylor et al. (US Pat. 5,001,048).

Clark et al., Kipling et al., and Nelson et al. teach sensor devices, as discussed above. However, the references do not teach the use of reference electrodes or an interdigitated electrode assembly.

Taylor et al. teach an electrical biosensor for analyte determination. In one embodiment, a single chip design is used, wherein the transducer is a quartz or glass substrate containing two terminal interdigitated electrodes. A receptor (which may be an antibody) containing membrane is in contact with the electrodes. A current is applied across the electrodes creating an electric field, such that a change in impedance results upon binding of an analyte to its receptor. The impedance is measured and is indicative of analyte concentration in the sample. In another embodiment, a double chip design may be used. This biosensor includes a non-receptor (reference) membrane and a receptor containing membrane, wherein the membranes are attached to different electrode surfaces, and impedance measured from control membrane is considered as a background signal. A barrier, which may be comprised of an insulator, is located between the reference and receptor-containing electrode to inhibit current flow between the two surfaces. It is once again inherent that the power supply is AC or DC.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the reference electrodes and insulating layer, as well as the interdigitated electrode assembly of Taylor et al. with the modified sensor of Clark et al., Kipling et al., and Nelson et al. One would have been motivated to use a reference electrode in an insulating layer to determine a background signal, wherein a difference from background can be used as an

indication of the analyte of interest. Further, an insulator provides the advantage of preventing current flow between the reference electrode and sensor electrode, which results in a contamination of assay results. It would have also been obvious to use an interdigitated electrode assembly because Clark et al. state that a number of electrode configurations can be used with the device of their reference. Further, the configuration depicted in figure 4 of the reference resembles an interdigitated assembly, and one would expect such a configuration to work with their sensor.

11. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Clark et al. (US Pat. 5,194,133) in view of Kipling et al. (US Pat. 5,374,521) and Nelson et al. (US Pat. 6,074,827) as applied to claims 10, 12-13, 16, and 20-21 above, and further in view of Stetter et al. (US Pat. 5,567,301).

Clark et al., Kipling et al., and Nelson et al. teach sensor devices, as discussed above. However, the references do not teach the use of an AC source.

Stetter et al. teach a biosensor comprising two spaced metal electrodes, wherein at least one antibody is disposed on and/or between the two electrodes. The sensor also comprises impedance detection means for measuring the impedance between the two electrodes (cols. 3-4). Since figure 2 shows the impedance as a function of the AC frequency, the presence of an AC power source for the production of an electric field across the electrodes is inherent.

It would have been *prima facie* obvious to use the AC power source of Stetter et al. with the sensor of Clark et al., Kipling et al., and Nelson et al. because the use of AC impedance is very well known in the art, and one would have known that an AC source could have easily been substituted for the DC source of Clark et al. with a reasonable expectation of success.

12. Claims 11 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over van Gerwen et al. (WO 97/21094) and Nelson et al. (US Pat. 6,074,827) as applied to claims 10, 12-18, and 21-28 above, and further in view of Taylor et al. (US Pat. 5,374,521).

Van Gerwen et al. and Nelson et al. teach a sensor device, as previously discussed. However, the references do not teach reference electrodes or insulation.

Taylor et al. teach an electrical biosensor for analyte determination. In one embodiment, a single chip design is used, wherein the transducer is a quartz or glass substrate containing two terminal interdigitated electrodes. A receptor (which may be an antibody) containing membrane is in contact with the electrodes. A current is applied across the electrodes creating an electric field, such that a change in impedance results upon binding of an analyte to its receptor. The impedance is measured and is indicative of analyte concentration in the sample. In another embodiment, a double chip design may be used. This biosensor includes a non-receptor (reference) membrane and a receptor containing membrane, wherein the membranes are attached to different electrode surfaces, and impedance measured from control membrane is considered as a background signal. A barrier, which may be comprised of an insulator, is located between the reference and receptor-containing electrode to inhibit current flow between the two surfaces. It is once again inherent that the power supply is AC or DC.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the reference electrodes and insulating layer of Taylor et al. with the modified sensor of Van Gerwen et al. and Nelson et al. because the use of a reference electrode in an insulating layer allows the determination of a background signal, wherein a difference from background can be used as an indication of the analyte of interest. Further, an insulator provides

the advantage of preventing current flow between the reference electrode and sensor electrode, which results in a contamination of assay results.

Response to Arguments

13. Applicant's arguments filed 6/14/04 have been fully considered and are persuasive to overcome the rejections under 35 USC 112, as well as the obviousness double patenting rejections and the 103 rejection over Krulevitch, but they are not persuasive to overcome the remaining rejections under 35 USC 103.

14. Applicant first argues that van Gerwen does not teach beads coated with antibodies, to which the examiner acquiesces; however, Nelson is relied upon to cure this deficiency. Further, the van Gerwen reference does indeed teach the use of an impedance sensor. Although applicant may be correct in asserting that the reference does not teach an impedance sensor that measures a change in impedance between "said pair of spaced electrodes with said beads coated with antibodies amplifying the change in impedance," this is a process limitation that does not merit patentable weight in claims drawn to an apparatus. The combination of references teaches all the components of the device, and therefore render the claims to which they were applied obvious. Also, while applicant may be correct in asserting that Nelson does not teach all the components of the device, as a secondary reference, it is not required to do so, and the reference is only relied upon to cure the deficiencies in the primary reference.

15. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge

generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one would have been motivated to use the antibody-coated beads of Nelson et al. with the device of Van Gerwen et al. because Nelson teaches the use of these coated beads in fluidic systems having channels, and the use of these beads to bind the pathogens of Van Gerwen would allow for an even more noticeable difference in the impedance measurements between when pathogen is present and when it is not.

16. Applicant argues that Clark does not teach beads coated with antibodies, to which the examiner acquiesces; however, Nelson is relied upon to cure this deficiency. Further, the Clark does indeed teach the use of an impedance sensor. Although applicant may be correct in asserting that the reference does not teach an impedance sensor that measures a change in impedance between "said pair of spaced electrodes with said beads coated with antibodies amplifying the change in impedance," this is a process limitation that does not merit patentable weight in claims drawn to an apparatus. The combination of references teaches all the components of the device, and therefore render the claims to which they were applied obvious. Also, while applicant may be correct in asserting that Nelson does not teach all the components of the device, as a secondary reference, it is not required to do so, and the reference is only relied upon to cure the deficiencies in the primary reference. It is noted that applicant has failed to address Kipling in any appreciable manner.

17. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching,

suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one would have been motivated to use the antibodies on the surfaces of the electrode as taught by Kipling et al. with the device of Clark et al. because Kipling teaches that any number of biomolecules can be used on the electrode surface. Therefore, depending on the analyte one wishes to detect, one would have known that a number of receptors could have been placed on the electrodes of Clark et al. with a reasonable expectation of success. In addition, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to place the electrode pair on the same side of the microchannel, since it has been held that rearranging parts of an invention involves only routine skill in the art. *In re Japikse*, 86 USPQ 70. Also, the placement of the electrodes on a bottom surface of the microchannel would have been obvious because it simply represents an optimization of the device or a rearrangement of the parts of the device, which one would have had a reasonable expectation of success in using. It would have further been obvious to use the antibody-coated beads of Nelson et al. with the modified device of Clark et al. and Kipling et al. because Nelson teaches the use of these coated beads in fluidic systems having channels, and the use of these beads to bind the pathogens of interest would allow for an even more noticeable difference in the impedance measurements between when pathogen is present and when it is not.

18. Applicant's arguments with respect to the combination of Taylor or Stetter with Clark, Kipling, and Nelson appears to be based upon the premise that the latter 3 references do not form the basis of a proper 103 rejection, a position that has already been addressed and found

unconvincing. Similarly, applicant's arguments with respect to the combination of Taylor with van Gerwen and Nelson appears to be based upon the premise that van Gerwen and Nelson do not form the basis of a proper 103 rejection, which has also been previously addressed and found unconvincing.

Conclusion

Claims 10-28 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kartic Padmanabhan whose telephone number is 571-272-0825. The examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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06/25/04